Amendment to the Claims:

This listing of claims will replace all prior versions, and listing, of claims in the application.

Listing of Claims:

1. (currently amended) A virtual library of possible combinatorially derived product molecules which can be searched for product molecules having desired properties without the necessity of generating the product structures during the search, generated by the following process:

[[a.]] a) ~~Creating~~ creating one or more files identifying one or more combinatorial reactions for one or more core structures;

[[b.]] b) ~~Creating~~ creating separate structural variation files (associated with the reaction identifying files) in which are listed together the structural variations representative of those reactants which will react at each variation site of each combinatorial reaction;

[[c.]] c) ~~Associating~~ associating with each structural variation, data, characterizing each structural variation including:

(1) ~~Characterization~~ characterizing data, taking into account when necessary the structures of the cores with which the structural variations would be combined in the listed combinatorial syntheses, which has not been derived from the application of ~~validated molecular structural descriptors~~ molecular structural descriptors, validated as possessing a neighborhood property; and

(2) ~~Characterizing~~ characterizing data, taking into account when necessary the structures of the cores with which the structural variations would be combined in the listed combinatorial syntheses, which has been derived from applying ~~validated molecular structural descriptors~~ molecular structural descriptors, validated as possessing a neighborhood property, to the structural variations.

2. (currently amended) A virtual library of possible combinatorially derived product molecules which can be searched for product molecules having desired properties without the necessity of generating the product structures during the search, generated by the following process:

[[a.]] a) creating one or more files identifying one or more combinatorial reactions for one or more core structures [[:]] ;

[[b.]] b) creating separate structural variation files (associated with the reaction identifying files) in which are listed together the structural variations representative of those reactants which will react at each variation site of each combinatorial reaction [[:]] ;

[[c.]] c) associating with each structural variation, data, characterizing each structural variation including:

(1) [[.]] characterizing data, taking into account when necessary the structures of the cores with which the structural variations would be combined in the listed combinatorial syntheses [[.]] , which has not been derived from the application of ~~validated molecular~~

~~structural descriptors~~ molecular structural descriptors, validated as possessing a neighborhood property [[:]] ; and

(2) [[.]] characterizing data, taking into account when necessary the structures of the cores with which the structural variations would be combined in the listed combinatorial syntheses [[.]] , which has been derived from applying ~~validated molecular structural descriptors~~ molecular structural descriptors, validated as possessing a neighborhood property, to the structural variations [[:]] ; and

[[d.]] d) associating with each core, data characterizing each core including:

(1). characterizing data which has not been derived from application of ~~validated molecular descriptors~~ molecular structural descriptors, validated as possessing a neighborhood property [[:]] ; and

(2) characterizing data which is derived by the following additional steps:

(a) selecting a first core [[:]] ;

(b) [[.]] selecting an attachment bond on the core [[:]] ;

(c) topomerically aligning the core [[:]] ;

(d) characterizing the core with CoMFA fields and the coordinates of the end points of the other attachment bonds [[:]] ;

(e) repeating steps (b) through (d) for all attachment bonds on the core [[:]] ;

(f) selecting a next core [[:]] ; and

(g) repeating steps (b) through (1') for all cores.

3. (currently amended) A virtual library of possible combinatorially derived product molecules which can be searched for product molecules having desired properties without the necessity of generating the product structures during the search, generated by the following process:

[[a.]] a) defining chemical transformations and reagents and cores to be used to generate product molecules [[:]] ; and

[[b.]] b) using appropriate molecular descriptors to precalculate characteristics of the component parts of all possible product molecules.

4. (withdrawn) A screening library designed by a computer-based method which selects the screening library molecules from those molecules which could be created by all combinatorial arrangements of specified structural variations and a common core molecule comprising the following steps:

a. generating a virtual library by:

(1). creating one or more files identifying one or more combinatorial reactions for one or more core structures;

(2). creating separate structural variation files (associated with the reaction identifying files) in which are listed together the structural variations representative of those reactants which will react at each variation site of each combinatorial reaction;

(3). associating with each structural variation, data, characterizing each structural variation including:

(a). characterization data, taking into account when necessary the

structures of the cores with which the structural variations would be combined in the listed combinatorial syntheses, which has not been derived from the application of validated molecular structural descriptors; and

(b). characterizing data, taking into account when necessary the structures of the cores with which the structural variations would be combined in the listed combinatorial syntheses, which has been derived from applying validated molecular structural descriptors to the structural variations;

b. identifying in the virtual library all possible combinatorial product molecules which could result from the specified reactants and selected core molecules;

c. selecting from all possible combinatorial product molecules a product molecule for inclusion in the subset;

d. using a validated molecular descriptor appropriate to whole molecules with which the Virtual Library was generated, removing from the set of all remaining molecules those molecules falling within a chosen neighborhood distance of the selected molecule;

e. using a validated molecular descriptor appropriate to the structural variations with which the Virtual Library was generated, removing from the set of all remaining product molecules those molecules formed from structural variations falling within a chosen neighborhood distance of the structural variations of the selected molecule;

f. selecting from the set of all product molecules remaining after step **e** a product molecule for inclusion in the subset;

g. repeating steps **d** through **f** until no additional product molecules remain to be selected in step **f**; and

h. Outputting a list of the selected subset and/or the structural variations from which the subset can be formed.

5. (withdrawn) A screening library designed by a computer-based method which selects the screening library molecules from those molecules which could be created by all combinatorial arrangements of specified structural variations and core molecules comprising the following steps:

a. generating a virtual library by:

(1). creating one or more files identifying one or more combinatorial reactions for one or more core structures;

(2). creating separate structural variation files (associated with the reaction identifying files) in which are listed together the structural variations representative of those reactants which will react at each variation site of each combinatorial reaction;

(3). associating with each structural variation, data, characterizing each structural variation including:

(a). characterization data, taking into account when necessary the structures of the cores with which the structural variations would be combined in the listed combinatorial syntheses, which has not

been derived from the application of validated molecular structural descriptors; and

(b). characterizing data, taking into account when necessary the structures of the cores with which the structural variations would be combined in the listed combinatorial syntheses, which has been derived from applying validated molecular structural descriptors to the structural variations;

b. selecting from all possible cores a core upon which to base the subset;

c. using a validated molecular descriptor appropriate to cores, selecting from the set of all possible cores those core molecules falling within the neighborhood distance of the selected core molecule;

d. identifying all possible combinatorial product molecules which could result from the specified reactants and selected core molecules;

e. selecting from all possible combinatorial product molecules a product molecule for inclusion in the subset;

f. using a validated molecular descriptor appropriate to whole molecules with which the Virtual Library was generated, removing from the set of all remaining molecules those molecules falling within a chosen neighborhood distance of the selected molecule;

g. using a validated molecular descriptor appropriate to the structural variations with which the Virtual Library was generated, removing from the set of all remaining product molecules those molecules formed from structural variations falling within

a chosen neighborhood distance of the structural variations of the selected molecule;

h. selecting from the set of all product molecules remaining after step **g** a product molecule for inclusion in the subset;

i. repeating steps **f** through **h** until no additional product molecules remain to be selected in step **h**; and

j. Outputting a list of the selected subset and/or the structural variations and cores from which the subset can be formed.

6. (withdrawn) The use of a subset of molecules, which could be made in a combinatorial synthesis of specified reactants and common core, to specify the compounds to be synthesized and tested in appropriate assays, said subset being selected by the following computer-based method:

a. generating a virtual library by:

(1). creating one or more files identifying one or more combinatorial reactions for one or more core structures;

(2). creating separate structural variation files (associated with the reaction identifying files) in which are listed together the structural variations representative of those reactants which will react at each variation site of each combinatorial reaction;

(3). associating with each structural variation, data, characterizing each structural variation including:

(a). characterization data, taking into account when necessary the

structures of the cores with which the structural variations would be combined in the listed combinatorial syntheses, which has not been derived from the application of validated molecular structural descriptors; and

(b). characterizing data, taking into account when necessary the structures of the cores with which the structural variations would be combined in the listed combinatorial syntheses, which has been derived from applying validated molecular structural descriptors to the structural variations;

b. identifying in the virtual library all possible combinatorial product molecules which could result from the specified reactants and selected core molecules;

c. selecting from all possible combinatorial product molecules a product molecule for inclusion in the subset;

d. using a validated molecular descriptor appropriate to whole molecules with which the Virtual Library was generated, removing from the set of all remaining molecules those molecules falling within a chosen neighborhood distance of the selected molecule;

e. using a validated molecular descriptor appropriate to the structural variations with which the Virtual Library was generated, removing from the set of all remaining product molecules those molecules formed from structural variations falling within a chosen neighborhood distance of the structural variations of the selected molecule;

f. selecting from the set of all product molecules remaining after step **e** a product molecule for inclusion in the subset;

g. repeating steps **d** through **f** until no additional product molecules remain to be selected in step **f**; and

h. Outputting a list of the selected subset and/or the reactants from which the subset can be formed.

7. (withdrawn) The use of a subset of molecules, which are most likely to have the same type of activity as a molecule of interest and selected from those which could be made in a combinatorial synthesis from specified reactants and a common core molecule, to specify the compounds to be synthesized and tested in appropriate assays, said subset being selected by the following computer-based method:

a. generating a virtual library by:

(1). creating one or more files identifying one or more combinatorial reactions for one or more core structures;

(2). creating separate structural variation files (associated with the reaction identifying files) in which are listed together the structural variations representative of those reactants which will react at each variation site of each combinatorial reaction;

(3). associating with each structural variation, data, characterizing each structural variation including:

(a). characterization data, taking into account when necessary the structures of the cores with which the structural variations would

be combined in the listed combinatorial syntheses, which has not been derived from the application of validated molecular structural descriptors; and

(b). characterizing data, taking into account when necessary the structures of the cores with which the structural variations would be combined in the listed combinatorial syntheses, which has been derived from applying validated molecular structural descriptors to the structural variations;

b. identifying in the virtual library all possible combinatorial product molecules which could result from the specified reactants and selected core molecules;

c. selecting from all possible combinatorial product molecules a product molecule for inclusion in the subset;

d. characterizing the molecule of interest with both a validated molecular structural descriptor appropriate to whole molecules with which the virtual library was generated and with a validated molecular structural descriptor appropriate to structural variations with which the virtual library was generated;

e. using the same validated molecular descriptor appropriate to whole molecules, selecting the set of all possible molecules whose descriptor values fall within a chosen neighborhood distance of the selected molecule, and using the same validated molecular descriptor appropriate to structural variations, selecting the set of all possible molecules whose descriptor values fall within a chosen neighborhood distance of the selected molecule; and

f. Ouputting a list of the selected subset and/or the reactants from which the subset can be formed.

8. (withdrawn) The use of a subset of molecules, which are most likely to have the same type of activity as a molecule of interest and selected from those which could be made in a combinatorial synthesis from specified reactants and a common core molecule, to specify the compounds to be synthesized and tested in appropriate assays, said subset being selected by the following computer-based method:

a. generating a virtual library by:

(1). creating one or more files identifying one or more combinatorial reactions for one or more core structures;

(2). creating separate structural variation files (associated with the reaction identifying files) in which are listed together the structural variations representative of those reactants which will react at each variation site of each combinatorial reaction;

(3). associating with each structural variation, data, characterizing each structural variation including:

(a). characterization data, taking into account when necessary the structures of the cores with which the structural variations would be combined in the listed combinatorial syntheses, which has not been derived from the application of validated molecular structural descriptors; and

(b). characterizing data, taking into account when necessary the

structures of the cores with which the structural variations would be combined in the listed combinatorial syntheses, which has been derived from applying validated molecular structural descriptors to the structural variations;

b. identifying in the virtual library all possible combinatorial product molecules which could result from the specified reactants and selected core molecules;

c. selecting from all possible combinatorial product molecules a product molecule for inclusion in the subset;

d. characterizing the molecule of interest with a combination validated molecular descriptor, characterizing both whole molecule and structural variation features, with which the Virtual Library was generated;

e. using the same validated molecular descriptor, selecting the set of all possible molecules whose descriptor values fall within a chosen neighborhood distance of the selected molecule; and

f. Ouputting a list of the selected subset and/or the reactant from which the subset of molecules can be formed.

9. (withdrawn) The use of a subset of molecules, which could be made in a combinatorial synthesis of specified reactants and core molecules. to specify the compounds to be synthesized and tested in appropriate assays. said subset being selected by the following computer-based method:

a. generating a virtual library by:

(1). creating one or more files identifying one or more combinatorial reactions

for one or more core structures:

(2). creating separate structural variation files (associated with the reaction identifying files) in which are listed together the structural variations representative of those reactants which will react at each variation site of each combinatorial reaction:

(3). associating with each structural variation. data. characterizing each structural variation including:

(a). characterizing data. taking into account when necessary the structures of the cores with which the structural variations would be combined in the listed combinatorial syntheses. which has not been derived from the application of validated molecular structural descriptors: and

(b) characterizing data. taking into account when necessary the structures of the cores with which the structural variations would be combined in the listed combinatorial syntheses. which has been derived from applying validated molecular structural descriptors to the structural variations:

b. selecting from all possible cores a core upon which to base the subset:

c. using a validated molecular descriptor appropriate to cores. selecting from the set of all possible cores those core molecules falling within a chosen neighborhood distance of the selected core molecule:

d. identifying all possible combinatorial product molecules which could result from the specified structural variations and selected core molecules:

e. selecting from all possible combinatorial product molecules a product molecule for inclusion in the subset:

f. using a validated molecular descriptor appropriate to whole molecules with which the virtual library was generated, removing from the set of all remaining molecules those molecules falling within a chosen neighborhood distance of the selected molecule:

g. using a validated molecular descriptor appropriate to the structural variations with which the virtual library was generated. removing from the set of all remaining product molecules those molecules formed from structural variations falling within a chosen neighborhood distance of the structural variations of the selected molecule:

h. selecting from the set of all product molecules remaining after step if a product molecule for inclusion in the subset:

i. repeating steps f through h until no additional product molecules remain to be selected in step b: and

j. outputting a list of the selected subset and/or the structural variations and cores from which the subset can be formed.

10. (new) A virtual library of component parts of molecules and their characteristics in which all possible product molecules combinatorially derived from the component parts can be searched, without the necessity of generating the product structures during the search, for product

molecules having desired properties by searching through only a combination of the descriptors of the component parts of the product molecules, generated by the following process:

a) defining chemical transformations and reagents and cores to be used to specify possible product molecules: and

b) using appropriate molecular descriptors, validated as possessing a neighborhood property, to precalculate characteristics of the component parts of all possible product molecules.

11. (new) A virtual library of structural variations, cores, and their associated molecular structural descriptors, which can be searched for product molecules derived from the combinatorial assembly of the structural variations and cores having desired properties, by combining descriptors of the structural variations and cores to generate descriptors representative of the product molecules, without the necessity of generating the product structures during the search, generated by the following process:

a) creating one or more files identifying one or more combinatorial reactions for one or more core structures;

b) creating separate structural variation files, associated with the reaction identifying files, in which are listed together the structural variations representative of those reactants which will react at each variation site of each combinatorial reaction;

c) associating with each structural variation, data, characterizing each structural variation including:

(1) characterizing data, which has not been derived from applying at least one molecular structural descriptor, validated as possessing a neighborhood

property, to the structural variations, taking into account when necessary the structures of the cores with which the structural variations would be combined in the combinatorial syntheses; and

(2) characterizing data, which has been derived from applying at least one molecular structural descriptor, validated as possessing a neighborhood property, to the structural variations taking into account to the extent appropriate for application of the descriptor the structures of the cores with which the structural variation would be combined in the combinatorial syntheses.

12. (new) A virtual library of structural variations, cores, and their associated molecular structural descriptors, which can be searched for product molecules derived from the combinatorial assembly of the structural variations and cores having desired properties, by combining descriptors of the structural variations and cores to generate descriptors representative of the product molecules, without the necessity of generating the product structures during the search, generated by the following process:

a) creating one or more files identifying one or more combinatorial reactions for one or more core structures;

b) creating separate structural variation files, associated with the reaction identifying files, in which are listed together the structural variations representative of those reactants which will react at each variation site of each combinatorial reaction;

c) associating with each structural variation, data, characterizing each structural variation including:

(1) characterizing data, which has not been derived from applying at least one molecular structural descriptor, validated as possessing a neighborhood property, to the structural variations, taking into account when necessary the structures of the cores with which the structural variations would be combined in the combinatorial syntheses; and

(2) characterizing data, which has been derived from applying at least one molecular structural descriptor, validated as possessing a neighborhood property, to the structural variations taking into account to the extent appropriate for application of the descriptor the structures of the cores with which the structural variation would be combined in the combinatorial syntheses; and

d) associating with each core, data characterizing each core including:

(1). characterizing data which has not been derived from application of molecular descriptors, validated as possessing a neighborhood property; and

(2) characterizing data which is derived by the following additional steps:

(a) selecting a first core;

(b). selecting an attachment bond on the core;

(c) topomerically aligning the core;

(d) characterizing the core with CoMFA fields and the coordinates of the end points of the other attachment bonds;

(e) repeating steps (b) through (d) for all attachment bonds on the core;

(f) selecting a next core; and

(g) repeating steps (b) through (1') for all cores.

13. (new) A system for identifying from a virtual library of structural variations, cores, and their associated molecular structural descriptors, product molecules derived from the combinatorial assembly of the structural variations and cores having desired properties, without the necessity of generating the product structures during the search, comprising:

a) a general purpose computer further comprising:

(1) input devices;

(2) a central processing unit;

(3) random access memory;

(4) additional memory means for storing and accessing data; and

(5) output devices; and

b) a virtual library stored in accessible memory of structural variations, cores, and their associated molecular structural descriptors, which can be searched for product molecules derived from the combinatorial assembly of the structural variations and cores having desired properties, by combining descriptors of the structural variations and cores to generate descriptors representative of the product molecules, without the necessity of generating the product structures during the search, generated by the following process:

(1) creating one or more files identifying one or more combinatorial reactions for one or more core structures;

(2) creating separate structural variation files, associated with the

reaction identifying files, in which are listed together the structural variations representative of those reactants which will react at each variation site of each combinatorial reaction;

(3) associating with each structural variation, data, characterizing each structural variation including:

(a) characterizing data, which has not been derived from applying at least one molecular structural descriptor, validated as possessing a neighborhood property, to the structural variations, taking into account when necessary the structures of the cores with which the structural variations would be combined in the combinatorial syntheses; and

(b) characterizing data, which has been derived from applying at least one molecular structural descriptor, validated as possessing a neighborhood property, to the structural variations taking into account to the extent appropriate for application of the descriptor the structures of the cores with which the structural variation would be combined in the combinatorial syntheses.